DEPARTMENT OF THE NAVY
NAVAL MEDICAL CENTER
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SAN DIEGO, CALIFORNIA 92134-5000

IN REPLY REFER TO:
NAVMEDCEN SDIEGOINST 6500.9
KCA

12 JUL 2001

NAVMEDCEN SDIEGO INSTRUCTION 6500.9

From: Commander

Subj: HUMAN CLINICAL INVESTIGATION PROGRAM, INSTITUTIONAL REVIEW BOARD AND THE PROTECTION OF HUMAN SUBJECTS

Ref: (a) Code of Federal Regulations, Title 32 (National Defense), Part 219 (32 CFR 219)
(b) Code of Federal Regulations, Title 45 (Public Welfare, Department of Health and Human Services, National Institutes of Health, Office for Protection from Research Risks), Part 46 (45 CFR 46)
(c) The Belmont Report
(d) United States Code, Title 10 (Armed Forces), Section 980 (10 USC 980)
(e) DOD Directive 3216.2
(f) Office of the Secretary of Defense memo of 10 Jun 93
(g) DOD Office of General Council memo of 2 Oct 97
(h) SECNAVINST 3900.39B
(i) BUMEDINST 6000.12A
(j) BUMEDINST 6710.69
(k) NSHS BETHESDAINST 6000.41B
(l) NAVMEDCEN SDIEGOINST 1600.2
(m) NAVMEDCEN SDIEGOINST 6470.2G
(n) NAVMEDCEN SDIEGOINST 6470.6C
(o) NAVMEDCEN SDIEGOINST 6710.19

Encl: (1) General Requirements for Informed Consent
(2) First Party Consent Form Template
(3) Third Party Consent Form Template
(4) Privacy Act Statement
(5) California Experimental Subjects Bill Of Rights
(6) Waiver of Modification of Informed Consent
(7) Research Protocol Continuing Review Report
(8) Clinical Investigation Completion Report
(9) What Is And Is Not A Clinical Investigation
(10) Categories of Research That May Be Expedited
(11) Categories Of Research That May Be Exempt
(12) Instructions for Human Use Research Proposal
(13) Human Use Research Proposal Template
(14) Adverse Event Report
(15) Table of Acronyms

1. Purpose. To establish the Institutional Review Board (IRB) at Naval Medical Center, San Diego (NMCSD) and delineate its

responsibilities for protecting the rights and welfare of human subjects participating in clinical investigation and research projects, per references (a) through (o).

2. Cancellation. NAVMEDCEN SDIEGOINST 6500.3B, NAVMEDCEN SDIEGOINST 6500.4E, NAVMEDCEN SDIEGOINST 6500.5D, and NAVMEDCEN SDIEGOINST 6500.8.

3. Definitions

a. Clinical Investigation. From reference (k), "A research program, project, task, test, experiment, record review, evaluation, or similar undertaking that uses data collected from Department of Defense (DOD) health care beneficiaries, laboratory animals, or *in vitro* to study the maintenance of health or the prevention, alleviation or cure of disease, and whose primary purpose is designed with the intent to develop or contribute to generalized knowledge."

b. Human Subject. From reference (h), "A living person from whom a researcher obtains data through interaction with the individual, or the individual's records, including both physical procedures and manipulations of the subject or the subject's environment. The term "human subject" as used in this instruction does not apply to those military or civilian personnel who are professionally qualified by training and experience and specifically assigned to participate in research, testing and evaluation by virtue of such qualification, such as test pilots, test parachutists, test drivers and test engineers."

c. Investigator. The Principal Investigator (PI) is the federal employee responsible for developing and submitting the research protocol and ensuring that the work is properly conducted. One or more Associate Investigators (AI) may collaborate with the PI in conducting the research protocol. Sub-investigators are individuals who will be trained in the specifics of the protocol and on how to perform the informed consent process from prospective subjects. The PI will be responsible for providing training to all sub-investigators.

d. Minimal Risk. From reference (a), "The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests."

e. Protocol. A formal written plan that specifies the manner in which a clinical investigation is to be conducted.

f. Risk. From reference (h) "The possibility of harm (physical, psychological, sociological, or other) as a consequence of any act or omission that goes beyond the application of established and accepted methods or procedures which are in an individual's best interest, or increases the possibility of harm inherent in his/her daily life or in his/her occupation or field of service." Research, by its very nature, may pose unforeseen risks.

4. Organization

a. Per reference (i), Naval Medical Department approval authority for the use of human subjects within the Clinical Investigation Program (CIP) is vested in the Commanding Officer (CO), Naval School of Health Sciences (NSHS), Bethesda. Per reference (k), CO, NSHS, Bethesda, via the CIP Director, may annually delegate local approval authority to the Commander, NMCSD based on the results of annual on-site inspections.

b. An "Assurance" is a formal, written, binding commitment of Assurance of Compliance with the Federal Policy for the Protection of Human Subjects. References (a) and (f) require institutional Assurance to DOD. For the Navy CIP, per reference (k), NSHS Bethesda is responsible for approval of Assurance applications and for issuing a DOD Assurance number. Assurances from all investigators to the local institution are also required by reference (k). In the case of research sponsored by the Department of Health and Human Services (HHS)/National Institute of Health (NIH), institutional assurance to HHS is required by reference (b).

c. The IRB is appointed by the Commander, NMCSD, to evaluate the scientific merit and protection of human subjects for each research proposal, and provide recommendations regarding approval directly to the Commander.

d. The Radiation Safety Committee (RSC) and the Laser Use Committee (LUC) (established by references (n) and (m) respectively) are responsible for the review of all research that involves the use of radiation (RSC) or lasers (LUC). These committees will comment on the adequacy of training of the investigators in the use of radiation or lasers, and on the risk/benefit analysis, that justifies the investigational exposure of subjects. These comments, if available prior to the IRB meeting, will be considered by the full IRB. If the comments are not

available until after the IRB meeting, they will be considered by the IRB Chair (and if necessary brought back before the full IRB) prior to making a recommendation on approval of the protocol.

e. All protocols that have been approved by the IRB will be forwarded with the IRB's minutes and any other required documentation to Commander, NMCSD for final approval ("local approval"). From reference (k), a "certification" is "a written communication by an authorized official at an institution with a valid Assurance (normally the CO) verifying that a specific proposal for research has been reviewed and approved by the designated IRB and is favorably endorsed for implementation. This communication is accomplished by the Commander's approval of IRB minutes." In the case of research sponsored by the Department of Health and Human Services (HHS)/National Institute of Health (NIH), this communication is accomplished by a Certificate of Compliance Form (HHS 310). Certain categories of research are not authorized for "local approval," but rather must have the favorable endorsement of higher authority before implementation. Subjects cannot be enrolled in any research protocol until approval has been granted. Human research requiring higher authority approval:

(1) Per reference (i), Bureau of Medicine and Surgery (BUMED) HIV Program Branch (MED-02H) must approve Retrovirology research.

(2) Per reference (h), the Assistant Secretary of the Navy for Research, Development and Acquisition must approve certain research, including research that is classified, involves severe and unusual intrusions or involves potential embarrassment to the Navy.

5. IRB Membership

a. Composition. The IRB will be composed of not fewer than 10 members and sufficient alternate members to ensure appropriate representation and consistent availability of a quorum. The IRB will be sufficiently qualified through the experience and expertise of its membership to ensure qualified review of scientific and human subject issues. The IRB will not consist entirely of members of a single profession or gender. There must be at least one member whose primary concerns are non-scientific. There will be at least one member who is not otherwise affiliated with NMCSD and is not the immediate family member of someone affiliated with NMCSD, and who is not subject to the immediate authority of the Commander, NMCSD (unaffiliated member). IRB

members must be federal government employees and are not compensated beyond their usual government salary for IRB membership. The federal government provides liability coverage for IRB duties. Suggested membership:

Chair	Senior Medical Officer (Board Certified)
Members	Medical Corps Officer(s)
	Medical Service Corp Officer(s)
	Nurse Corps Officer(s)
	Chaplain Corps Officer
	Dental Corps Officer
	Hospital Corps Representative
	Pharmacist
	Statistician (ad hoc)
	Psychiatry/Psychology/Social Work Professional
	Judge Advocate General Corps Officer (ad hoc)
	Unaffiliated Member

Note: One individual may fulfill multiple representative roles.

b. Appointment

(1) Commander, NMCSD, will appoint the Chair, IRB. The Chair will be appointed by name, not position, and may not be a staff member of CID. The Chair will be reappointed annually and can only be removed by the Commander. It is desirable that the Chair be a senior officer with considerable clinical experience and a background in clinical investigation.

(2) Members of the IRB will be appointed by name, not position, by the Commander, NMCSD, after nomination by their Director, with concurrence of the Chair, IRB. Members will be appointed based on their expected contribution. Members will be re-appointed annually and can only be removed by the Commander. Care will be taken to ensure that overlapping terms will occur.

(3) The IRB may appoint consultants as ad hoc members to supplement its membership if it is determined that current members do not possess the specific knowledge required to competently assess a particular protocol. The ad hoc members will have no vote.

c. Voting. A quorum must be present to conduct an IRB meeting and will be composed of a majority of voting members. Alternate members will be called upon by the Chair as necessary to ensure the availability of a quorum and to ensure the appropriate fields of representation to conduct a meeting. A quorum must

include at least one physician and one member whose primary concerns are non-scientific. Only IRB members will be present in the room during voting. Investigators will not be present in the room during voting. Actions will be based on votes by a majority of voting members present in the room. Telephone and write in voting are not permitted. The Chair will vote only to break a tie. The Judge Advocate General Corps and any other ad hoc members will be non-voting members. All other regular and alternate IRB members present are full voting members.

d. The Chair, IRB will:

(1) Be familiar with references (a) through (o).

(2) Review proposals to determine endorsement under expedited review criteria or exempt from human subjects' regulation criteria as specified in reference (k).

(3) Conduct (or appoint one or more IRB members to conduct) and approve expedited review of new protocols or minor modifications to previously approved protocols meeting the criteria for such expedited review.

(4) Appoint, if desired, a primary reviewer for each protocol to thoroughly evaluate each proposal prior to the IRB meeting.

(5) Convene IRB meetings monthly, per references (a) through (o), and approve the minutes of IRB proceedings for the Commander's review.

(6) Determine conflict of interest for the purpose of excusing members from participation in initial or continuing reviews.

(7) Review and grant approval for revisions to research protocols that were approved by the IRB pending such revisions.

(8) Sign/initial original IRB-approved informed consent documents.

(9) Ensure that adverse event reports are reviewed at the next regular meeting of the IRB.

(10) Approve requests for emergency or compassionate use of investigational drugs, devices and biologics as allowed under

reference (o), and ensure that the approvals are reviewed at the next regular meeting of the IRB.

(11) Provide the official signature on Certificate of Compliance Form (HHS-310) when required.

(12) Prepare a Statement of Assurance when required by regulations to CIP NSHS Bethesda.

(13) Ensure that recommendations based on the annual site visit by CIP, NSHS Bethesda are implemented.

(14) Provide orientation and continuing education to IRB members on the protection of human subjects.

(15) Conduct periodic review of the administrative support services provided to the IRB and report the adequacy of such support services to Head, CID.

e. The Vice Chair, IRB will:

(1) Be an experienced IRB member appointed by the Chair.

(2) Be familiar with references (a) through (o).

(3) In the absence of the Chair, act as Chair.

(4) For proposals in which the Chair has a potential conflict of interest, act as Chair.

f. The Members of the IRB will:

(1) Review all proposals prior to regularly scheduled IRB meetings.

(2) Act as primary reviewers, prior to regularly scheduled IRB meetings, for any specific proposals assigned by the Chair. If required, reviewers may communicate with the investigator to request additional information.

(3) Attend scheduled meetings. If attendance is impossible, it is the responsibility of the member to contact the IRB administrative assistant to arrange for the attendance of an alternate. New members are required to observe two meetings before participating.

(4) Complete orientation and continuing education on the protection of human subjects, including familiarity with references (a) through (o).

(5) Excuse themselves from participation in IRB initial or continuing review of any project in which they have a conflict of interest, except to provide information requested by the IRB.

6. Initial IRB review of clinical investigation proposals

a. The IRB will review all clinical investigation proposals that involve Principal Investigators who are federal employees attached to NMCSD or its satellite facilities (all Navy Medical Treatment Facilities (MTF), dental treatment facilities and branch medical clinics in - Alaska, Arizona, California, Colorado, Hawaii, Idaho, Kansas, Montana, Nebraska, Nevada, New Mexico, North Dakota, Oregon, South Dakota, Utah, Washington, and Wyoming, and in Diego Garcia, Guam, Japan and Korea).

b. Scientific Adequacy. The IRB will review all clinical investigation proposals for scientific adequacy to include the following:

(1) Background, objectives, and importance to Navy Medicine.

(2) Literature search being sufficiently extensive to provide reasonable expectation of detecting prior accomplishment of the proposed study.

(3) Study design, specific procedures and time schedule.

(4) Choice of population characteristics.

(5) Sample size determination and proposed statistical analysis of data.

(6) Budget request.

(7) Impact on other departments (e.g., radiology, pharmacy, and laboratory).

(8) The requirement, if any, for supporting Memorandum of Understanding (MOU), Cooperative Research and Development Agreements (CRADAs) and/or other agreements.

(9) Per reference (j), investigational drugs, devices or biologics to be used, including supporting forms required by the Food and Drug Administration (FDA).

(10) Investigator's brochure from sponsor, if any.

(11) Data collection sheets.

(12) Research team qualifications and composition, with one federal employee (staff or trainee) at NMCSD designated as the principal investigator and other investigators listed as associate investigators or sub-investigators.

c. Protection of Human Subjects. The IRB will review all clinical investigation proposals involving the use of human subjects as follows:

(1) The study must contribute to human benefit and have reasonable prospects of yielding important results, which are not known to be obtainable by other methods or means of study.

(2) Only persons possessing the requisite scientific qualifications will conduct the study. Persons who conduct or assist in the study will exercise the highest degree of skill and care during all stages of the study.

(3) A risk category will be assigned, either minimal or greater than minimal as defined above.

(4) The number of human subjects will be kept to the minimum necessary to achieve the anticipated results.

(5) Selection of subjects must be equitable. In making this assessment the IRB will take into account the purposes of the research and the setting in which the research will be conducted. The IRB should be particularly cognizant of the special problems of research involving potentially vulnerable populations, such as children, pregnant women, mentally disabled persons, economically or educationally disadvantaged persons, and active duty members. Specific inclusion and exclusion criteria will be evaluated. For any group of subjects to be excluded, an explanation other than convenience must be stated.

(6) Only persons eligible for care in MTFs are eligible to be research subjects. During or after any study, medical or dental treatment, including hospitalization if necessary, will be provided to any subject who requires such treatment or hospitalization as a result of his/her participation in the study,

as soon as such need is recognized. Where appropriate, provisions will be made in advance for rapid medical evacuation of subjects to an adequate hospital facility, military or otherwise, in case of emergency.

(7) The subjects will have no physical or mental condition, which will make participation more hazardous for him or her than for a healthy person, unless such condition is a necessary prerequisite for the particular study involved. The use of a human subject with such a pre-existing condition must be specifically approved in advance for that particular protocol.

(8) Prisoners will not be used as subjects under any circumstances.

(9) Institutionalized mentally disabled persons will not be used as subjects if the proposed study is deemed to present more than minimal risk. The expedited review procedure may not be used for studies involving this special population. The term "institution," used in this sense, will not apply to medical or dental treatment facilities.

(10) Reference (d) stipulates that DOD appropriated funds may not be used for research involving human experimental subjects unless "the informed consent of the subject is obtained in advance" or, "in the case of research intended to be beneficial to the subject, the informed consent of the subject or a legal representative of the subject is obtained in advance." This has been interpreted, per reference (g), to mean that third party consent cannot be given to enroll subjects in studies in which the subject may be assigned to a group that would not provide the subject personal benefit.

(11) Reference (b) requires the IRB to determine that adequate provisions are made for soliciting the assent of children, when in the judgment of the IRB the children are capable of providing assent. Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

(12) Informed consent must be sought from each prospective subject or the subject's legally authorized representative. An investigator will seek consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence, especially of potentially vulnerable subjects per paragraph 6c(5)

above. The information that is given to the subject or the representative will be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(13) Reference (a) states that subjects must give informed consent to participate in human research and that information must be given "in language understandable to the subject." When the study subject population is expected to include non-English speaking people, the IRB will require a translated Informed Consent Document (ICD) to be prepared prior to study approval and for translators to be present during the consent process. Since informed consent is not a one-time event related to signing the ICD, but rather an ongoing dialogue between investigators and subjects, translation needs to be consistently available to meet this need. As a result of language and cultural differences, translation into a language other than the investigators' may still leave doubt about the subjects' true understanding. If the subject does not clearly understand the information presented, the subject's consent will not truly be informed. Persons who are felt by investigators not to be able to give true ongoing informed consent because of language differences will not be enrolled as research subjects. If non-English speaking subject is unexpectedly encountered, investigators will not have an approved written translation of the consent document and the subject may not be enrolled.

(14) The informed consent document must meet the requirements of references (a), (h), and (k) and include a Privacy Act Statement and a California Experimental Subjects Bill of Rights (See enclosures 1-5). Under certain circumstances, the requirement for a signed informed consent document may be waived or modified (See enclosure (6)).

(15) The degree of risk will never exceed that required by the urgency or importance of the objectives to which the study is related. Risks to subjects must be reasonable in relation to anticipated benefits, if any, to subjects, and to the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapy subjects would receive even if not participating in research). The IRB should not consider possible long-range effects of applying knowledge

gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(16) Proper preparations will be made, and adequate facilities provided, to protect the human subjects against all possibilities of injury, disability or death. The study will be conducted to avoid all unnecessary physical or mental discomfort, suffering or injury.

(17) No study will be initiated if there is any reason to believe that death or disabling injury is likely to occur as a result of participation. Sufficient animal or laboratory experiments must have been completed to provide assurance of reasonable safety of the proposed study prior to use.

(18) Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose the subjects to risk and, whenever appropriate, by using procedures already being performed for diagnostic or treatment purposes.

(19) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, per paragraph 6c(5) above, additional safeguards will be included in the study to protect the rights and welfare of these subjects.

(20) There will be no greater intrusion into the privacy of the subject than is necessary for the conduct of the study. There must be appropriate methods to maintain confidentiality with regard to the storage of subject identifiers and data, particularly when the information will be entered into an electronic data system.

(21) The person conducting the study and each member of the investigative team will be prepared to terminate the subject's participation at any stage if they have reason to believe that even though good faith, superior skill, and careful judgment are exercised that continuation is likely to result in injury, disability or death to the subject.

(22) For greater than minimal risk studies, a locally credentialed physician (or dentist in the case of a dental study) who is not part of the investigative team and has agreed to be responsible for medical monitoring will be named with the monitor's signature acknowledging the assignment. The appointment text should specify the monitor's duties, to include, but not

limited to, monitoring subject recruitment and enrollment, the consent process, data collection, adverse events and privacy. The monitor may recommend suspension of the study if necessary to the IRB.

(23) When research is conducted outside the United States involving the use of non-United States citizens as human subjects, the laws, customs and practices of the country in which research is conducted, or those required by these instructions, whichever are more stringent, will take precedence. The research will meet the same standards of ethics and safety that apply to research conducted within the United States involving United States citizens.

(24) An appropriate interval will be assigned for continuing review. Reference (a) states that "An IRB will conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year."

d. IRB Actions. Based on the initial review of clinical investigation proposals, the IRB will take one of the following actions:

(1) Recommend approval of the protocol (as submitted).

(2) Recommend approval of the protocol pending submission of specific modification.

(3) Defer recommendation for approval/disapproval of the protocol ("table" the protocol). A tabled protocol must be re-presented at a subsequent IRB meeting. A protocol can be deferred only twice; then it must be either approved or disapproved. Circumstances that would warrant deferral include:

(a) Member of investigative team required to answer questions is not present.

(b) Requires extensive revision.

(4) Disapprove the protocol, identifying the reasons for such action. An investigator may respond to an IRB recommendation for disapproval, and may submit a revised protocol for consideration at a later date. However, a final decision by the IRB to recommend disapproval of a proposal cannot be overturned by higher authority.

e. The PI, and sponsor, if any, must be notified in writing of the IRB action after the IRB minutes have been approved by the Commander, NMCSD.

7. Continuing Review

a. The IRB is required to conduct continuing review of all non-exempted, human subject research (including emergency one-time use of an investigational drug) at intervals appropriate to the degree of risk and at least annually, in order to verify continuing compliance with pertinent regulations and policy. The IRB will also review all requests for modifications to previously approved protocols.

b. Based on the continuing review of the research (enclosure (7)), the IRB will take one of the following actions:

(1) Continuation. Approval for continuation until the next scheduled continuing review.

(2) Continuation with modifications. Approval, pending submission of specific modifications, for continuation until the next scheduled continuing review.

(3) Place restrictions on a study. These restrictions may not be lessened or removed by any other echelon of command.

(4) Completion. When study objectives have been met and no subject follow-up is required, the study is considered completed. Enclosure (8) must be submitted by the PI to CID within 30 days of study completion. CID will forward a copy of the completion report to CIP NSHS Bethesda within 30 days of receipt.

(5) Suspension. A study may be suspended by the IRB, or unilaterally by the Chair, during evaluation of adverse events, infractions involving noncompliance with IRB requests for information, or for infractions involving human use guidelines. If unilaterally suspended by the Chair, the issue will be an agenda item at the next regularly scheduled IRB meeting. While a study is suspended, no further subjects may be enrolled, no funds may be used to support any further work on that study except as may be medically indicated for enrolled subjects, and investigators are not eligible for CIP funded travel related to that study. Studies will be automatically suspended if continuing review is not completed within 365 days from the date of initial approval or last continuing review (or shorter timeframe if

required by the IRB). A suspended study may be reinstated to a continuation status or modified to a completed status.

(6) Termination. A study may be terminated by the IRB or the investigators due to major or recurring minor adverse events, major or recurring minor noncompliance with human use or reporting requirements, lack of progress, or departure of the PI or critical AI. However, if enrolled subjects require future follow-up in accordance with the protocol, the study may not be terminated. In that case, the issues warranting termination should be presented by the Chair, IRB to the PI's CO via the chain of command for alternate means of resolution. Once a study is terminated, no further subjects may be enrolled, no funds may be used to support any further work on that study except as may be medically indicated for enrolled subjects, and investigators are no longer eligible for CIP funded travel related to that study. CID will forward a copy of the termination report to CIP NSHS Bethesda within 30 days of receipt.

c. All actions taken by the IRB relative to continuing review are reported in meeting minutes to the Commander, NMCSD. Higher authority cannot overturn any decision by the IRB to suspend or terminate a study.

d. The principal investigator and sponsor and regulatory agencies, if any, must be notified in writing of the IRB action after the IRB minutes have been approved by the Commander, NMCSD.

8. Non-CIP Projects. Reference (i) describes projects that do not qualify as CIP projects, such as process improvement questionnaires, case reports, literature reviews, establishment of registries, and epidemiological surveillance (See enclosure (9)). Such projects do not require reporting to NSHS Bethesda and are not eligible for travel funds from NSHS Bethesda. However, these projects still require IRB approval and continuing progress reports.

9. Expedited and/or Exempt Research. Per reference (k), certain categories of investigations may present either negligible or no apparent risk to subjects. In those cases, reference (a) authorizes reduced institutional oversight. However, the decision of whether a study qualifies for expedited review or is exempt from review is not left to investigator discretion, but rather to the Chair of the IRB. When a study has been determined to qualify for either expedited review, or to be exempt from the requirements for review, the protocol document and relevant IRB minutes must cite the specific regulatory criterion that pertains.

a. Expedited Research. Expedited initial and continuing review procedures are authorized by reference (a) for certain categories of research involving no more than minimal risk, and for minor changes in previously approved research during the period for which approval has been authorized. The review may be carried out by the IRB Chair, or by one or more experienced reviewers designated by the Chair from among IRB voting members. In reviewing the research, the reviewers may exercise all to the authorities of the IRB except recommend disapproval, since a recommendation for disapproval can only occur after non-expedited review. The results of expedited reviews will be reported in the minutes of the next scheduled IRB meeting. The categories of research that qualify for expedited review are specified in a list prepared by the Secretary, HHS, and published periodically in the Federal Register. A copy of the most current list is available from the Office for Human Research Protections, Department of Health and Human Services, 6100 Executive Boulevard, Suite 3B01, MSC-7507, Rockville, MD 20892-7507. At this time, the current list is available at: http://ohrp.osophs.dhhs.gov/humansubjects/guidance/expedited98.htm on the World Wide Web. (See enclosure (10)).

b. Exempt Research. Certain categories of research involving human subjects may be exempt from reference (a). Section 219.101(b) of reference (a) specifies those categories (See enclosure (11)). Such studies still require a protocol proposal (less the Application to Use Human Subjects), IRB approval and continuing progress reports.

c. The use of expedited and exempted categories is not mandatory. The IRB may elect to require full review for either or both categories of research. However, the following must receive full review:

(1) Studies involving third party consent.

(2) Studies requiring investigational new drug or new device applications to the FDA.

(3) Studies involving retroviral agents.

(4) Studies requiring Assistant Secretary of the Navy (Research, Development and Acquisition) approval.

10. Investigational Agents in Clinical Investigations. The use of investigational drugs, devices and biologicals in research protocols is governed by reference (j).

a. Investigational agents in research involve not only agents that are not FDA approved, but also agents that are FDA approved, but are being studied for a non-FDA approved ("off-label") indication, dose, route of administration or combination, even when such clinical use would be legal in individual patients.

b. Appropriate approval must be obtained for their use prior to initiation of a study. Investigational drugs and biologics require an Investigational New Drug (IND) number from the FDA. Investigational devices require an Investigational Device Exemption (IDE) number from the FDA. An IDE application will be filed for all such devices, even if the device may be a "non significant risk" device.

11. Emergency, One-Time Use of Investigational Agents. Such use is governed by reference (o).

12. Chairmen/Department Heads will:

a. Appoint a Departmental Research Coordinator.

b. Allow sufficient time for department members to conduct approved research protocols.

13. Departmental Research Coordinators will:

a. Be familiar with the applicable regulations regarding the conduct of human subject research to include, at a minimum, references (a) and (c) and this instruction.

b. Be familiar with protocol submission and IRB review processes at NMCSD.

c. Review all research protocols from their department, suggesting changes to PIs as appropriate, prior to submission for IRB review.

14. Investigators will:

a. Be familiar with the applicable regulations regarding the conduct of human subject research to include, at a minimum, references (a) and (c) and this instruction.

b. Submit enclosures (12) and (13) in the current CID format per the current CID Standard Operating Procedures.

c. Make application, when required, to the FDA for use of investigational drugs, devices or biologicals.

d. Ensure that no clinical investigation project involving human subjects is initiated or continued without appropriate review and approval per the provisions of this instruction.

e. Ensure that changes to an approved protocol, or of investigators attached to the study are submitted to the IRB for approval prior to initiation.

f. Ensure that adverse events or unanticipated problems which arise in the course of a study which may affect the rights and welfare of human subjects, are expeditiously reported to the IRB using enclosure (14), in addition to any other required reports (e.g., sponsors, FDA, OHRP).

g. Supply the IRB with all requested information including continuing review and completion reports.

h. Not abandon research projects or subjects. Investigators will inform the IRB of the pending transfer of the PI or critical associate investigators, including plans to care for enrolled subjects and complete the study.

15. Record Keeping. The IRB will prepare and maintain adequate documentation of its activities, including the following:

a. Copies of all research proposals (including emergency use) reviewed (including budgets and supporting documentation), approved consent documents, progress reports submitted by the investigator, reports of adverse events, and reports of significant new findings provided to subjects.

b. Minutes of all IRB meetings, including attendance, a succinct account of IRB discussion, actions taken by the IRB, and the vote on these actions, including the number of members voting for, against, and abstaining.

c. Records of Continuing Review activities.

d. Copies of all correspondence between the IRB and investigators, collaborators, sponsors and regulatory agencies.

e. A list of IRB members, identified by name, earned degrees, representative capacity, indications of experience sufficient to describe each member's chief anticipated contributions to IRB

deliberations, and any employment or other relationship between each member and the institution (e.g., full time employee, paid or unpaid consultant).

f. All records associated with human subjects in research will be retained permanently.

16. Establishment of a Second IRB. If the Chair, IRB or the Head, CID determines that workload or other factors support its utility, a second NMCSD IRB may be established. This IRB will be designated IRB II and the original IRB will be IRB I. The second IRB will be established and function in accordance with this instruction with the exception that the minimum membership is eight, including the Chair. It is also recommended that one member serve in common on both IRBs to ensure consistency in decision making and the application of regulations. The IRBs will function in parallel. Review authority over protocols may not be transferred between IRBs.

17. Administrative Support. Every command establishing an IRB is tasked with providing adequate space and personnel to support the IRB per reference (i). The CID is the administrative, technical, regulatory and material support unit for all aspects of the CIP at NMCSD. The CID will provide the following support to the IRB:

a. Review of proposals for administrative completeness and accuracy prior to submission to the IRB for action.

b. Administrative staff to assist with:

(1) Protocol formats.

(2) Consent documents.

(3) Budget and ordering of supplies budgeted through CID.

(4) Establishment of Cooperative Research and Development Arrangements (CRADAs), Memoranda of Understanding (MOUs) and similar arrangements with outside collaborators.

(5) Funding through the Henry M. Jackson Foundation or other outside sources of funding.

(6) Correspondence with the FDA regarding Investigational New Drug Applications and IDEs.

(7) Scheduling of IRB meetings.

(8) Distribution of proposals to be reviewed prior to IRB meetings.

(9) Meeting minutes.

(10) Record keeping per paragraph 17 above.

(11) Reporting requirements including reporting the following to NSHS, Bethesda:

(a) Assurance of compliance with the Federal Policy for the Protection of Human Subjects.

(b) IRB minutes.

(c) Complete study packages for new protocols approved.

(d) Changes to existing protocols including addition or deletion of investigators and approved modifications to the protocol.

(e) Reports pertaining to investigational agents completion, suspension and termination reports.

(f) Adverse event reports.

c. Reference materials including applicable instructions, SOPs, and continuing education materials.

d. Conference space for meetings.

e. Filing space and reproduction equipment.

18. Acronyms. Enclosure (15) lists the acronyms used with this instruction.

W. M. ROBERTS
Acting

Distribution:
Lists 1 and 3

TITLE 32--NATIONAL DEFENSE PART 219--PROTECTION OF HUMAN SUBJECTS

GENERAL REQUIREMENTS FOR INFORMED CONSENT

32 CFR 219.116
"Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

a. Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to

whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

b. Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(6) The approximate number of subjects involved in the study."

NAVAL MEDICAL CENTER
SAN DIEGO, CALIFORNIA 92134-5000

CONSENT *BY A SUBJECT* FOR VOLUNTARY PARTICIPATION IN A CLINICAL INVESTIGATION (RESEARCH) STUDY

1. I, _____, have been asked to voluntarily participate in a research project entitled, "_____," being conducted at the Naval Medical Center, San Diego by medical researchers from the Department(s) of _____.

2. The objective(s) or purpose(s) of this research project are to: _____.

3. I understand that my participation in this research project will be for a period of _____.

4. The procedure(s) for this project include: _____.

5. Specifically, I am aware that the experimental part(s) of this research project are _____.

6. A total of _____ subjects are expected to participate in this study.

7. The risks or discomforts which are possibly related to my participation in this study are as follows: _____.

7B. ***If applicable*** *insert* "I am aware that this study may involve risks to me which are currently unforeseeable. I am also aware that this study may involve risks, if applicable, to my unborn baby if I am or become pregnant. I am aware that I should promptly advise my doctor and the study researcher identified below if I am now pregnant, if I contemplate becoming pregnant, or if I become pregnant during my participation in the study. Further, I am also aware that I should promptly advise my doctor and the study researcher if I am now breastfeeding or contemplate breastfeeding my child during the course of this study."

8. I understand that my participation in this research project may or may not be of direct benefit to me personally. However, the results of this study may help the investigator gain

Subject's Initials: _____

IRB Approval Stamp/Seal Required

important knowledge about _____ or aid in the future medical evaluation or treatment of other patients.

9. The alternate procedure(s) or course of treatment, should I decide not to participate in this research study, has been explained to me as follows: _____.

10. In all publications and presentations resulting from this research study, information about me or my participation in this project will be kept in the strictest confidence and will not be released in any form identifiable to me personally. However, I realize that authorized personnel from the Navy Medical Department and from the Food and Drug Administration (FDA), where applicable, may have access to my research file in order to verify that my rights have been adequately protected.

11. I understand that I will not be financially compensated for my participation in this study.

12. If I suffer any injury directly related to my participation in this research study, immediate medical attention is available at the Naval Medical Center, San Diego, or at another closer medical treatment facility, if applicable. Any injury resulting from my participation in this study will be evaluated and treated in keeping with the benefits or care to which I am entitled under applicable Navy, other Department of Defense, and other state or Federal regulations.

13. If I have any questions regarding this research study, I may contact **Dr.**_____ at (phone). If I have any questions about my rights as an individual while participating in a research study at the Naval Medical Center, San Diego, I may contact **CDR Kenneth Earhart, MC, USN, Chairman, Committee for the Protection of Human Subjects at (619)532-8125, or CDR John Kelso, MC, USN, Head, Clinical Investigation Department at (619)532-8127.** If I believe that I have been injured as a result of my participation in this research study, I may contact **CDR Lynn McNees, JAGC, USN, Naval Medical Center, San Diego, Legal Department, at (619)532-6475.**

14. I understand that my participation in this project is entirely voluntary and that my decision not to participate will involve no penalty or loss of benefits to which I am entitled under applicable regulations. If I choose to participate, I am free to ask questions or to withdraw from the study at any time. If I should decide to withdraw from the research project, I will notify _____ at (phone) to ensure my timely removal from the study. My withdrawal will involve no prejudice to my future health care or any loss of rights or benefits to which I am otherwise entitled. Any new significant finding developed

during the course of this study which might affect my willingness to continue participation will be communicated to me.

14B. ***If applicable***: The investigator may terminate my participation in this study for the following reasons:

_____.

15. I understand that I am making a decision whether or not to participate in the research project described in the preceding sections subject to the conditions of participation described above. My signature indicates that I have decided to participate, having read and understood the information presented above and having been given the opportunity to ask any questions that I might have about the research study or my participation in the study. Further, my signature indicates that I have been provided with a copy of this consent document and a copy of a document entitled, "California Experimental Subject's Bill of Rights."

SIGNATURES AND **DATE** SIGNED: **PRINTED** OR **TYPED IDENTIFICATION:**

_____	_____
Patient / Subject (Date)	Name / Status / Sponsor's SSN
_____	_____
Witness (Date)	Name / Grade or Rank
_____	_____
Researcher/Investigator(Date)	Name / Grade or Rank

Subject's Initials: _____

IRB Approval Stamp/Seal Required

Enter Summarized Title; PI: Last name, First initial; #: (Protocol Number) *)

NAVAL MEDICAL CENTER

SAN DIEGO, CALIFORNIA 92134-5000

CONSENT *BY A THIRD PARTY* FOR VOLUNTARY PARTICIPATION IN A CLINICAL INVESTIGATION (RESEARCH) STUDY

1. I, _____, parent/legal guardian **(circle one)** of _____, daughter/son/ parent/other dependent **(circle one; OR specify relationship of other dependent: _____)** have been asked to voluntarily allow the participation of my dependent named above in a research project entitled, "_____" being conducted at the Naval Medical Center, San Diego by medical researchers from the Department(s) of _____.

2. The objective(s) or purpose(s) of this research project are to: _____.

3. I understand that my dependent's participation in this research project will be for a period of _____.

4. The procedure(s) for this project includes: _____.

5. Specifically, I am aware that the experimental part(s) of this research project are _____.

6. A total of _____ subjects are expected to participate in this study.

7. The risks or discomforts to my dependent which are possibly related to his or her participation in this study are as follows: _____.

7B. ***If applicable*** *insert* "I am aware that this study may involve risks to my dependent, which are currently unforeseeable. I am also aware that this study may involve risks, if applicable, to her unborn baby if she is or becomes pregnant. I am aware that my dependent or I should promptly advise my dependent's doctor and the study researcher identified below if she is now pregnant, if she contemplates becoming pregnant, or if she becomes pregnant during her participation in the study. Further, I am also aware that I or my dependent should promptly advise my doctor and the study researcher if she is now breastfeeding or contemplates breastfeeding her child during the course of this study."

Subject's Initials: _____

IRB Approval Stamp/Seal Required

Enter Summarized Title; PI: Last name, First initial; #: (Protocol Number) *)

8. I understand that my dependent's participation in this research project may be of direct benefit to her or to him personally. Further, the results of this study may help the investigator gain important knowledge about _____ or aid in the future medical evaluation or treatment of other patients.

9. The alternate procedure(s) or course of treatment, should I decide not to allow the participation of my dependent in this research study, has been explained to me as follows: _____. My dependent will receive standard medical treatment, decided on by his or her doctor and me.

10. In all publications and presentations resulting from this research study, information about my dependent or his or her participation in this project will be kept in the strictest confidence and will not be released in any form identifiable to my dependent personally. However, I realize that authorized personnel from the Navy Medical Department and from the Food and Drug Administration (FDA), where applicable, may have access to my dependent's research file in order to verify that his or her rights have been adequately protected.

11. I understand that my dependent will not be financially compensated for participation in this study.

12. If my dependent suffers any injury directly related to his or her participation in this research study, immediate medical attention is available at the Naval Medical Center, San Diego, or at another closer medical treatment facility, if applicable. Any injury resulting from my dependent's participation in this study will be evaluated and treated in keeping with the benefits or care to which my dependent is entitled under applicable Navy, other Department of Defense, and other state or Federal regulations.

13. If I have any questions regarding this research study, I may contact **Dr.**_____ at (phone). If I have any questions about my dependent's rights as an individual while participating in a research study at the Naval Medical Center, San Diego, I may contact **CDR Kenneth Earhart, MC, USN, Chairman, Committee for the Protection of Human Subjects at (619) 532-8125, or CDR John Kelso, MC, USN, Head, Clinical Investigation Department at (619) 532-8127.** If I believe that my dependent has been injured as a result of his or her participation in this research study, I may contact **CDR Lynn McNees, JAGC, USN, Naval Medical Center, San Diego, Legal Department, at (619)532-6475.**

Subject's Initials: _____

IRB Approval Stamp/Seal Required

Enter Summarized Title; PI: Last name, First initial; #: (Protocol Number) *)

14. I understand that my dependent's participation in this project is entirely voluntary and that my decision not to allow her or his participation will involve no penalty or loss of benefits to which my dependent is entitled under applicable regulations. If I choose to allow my dependent to participate, I am free to ask questions or to withdraw my dependent from the study at any time. If I should decide to withdraw my dependent from the research project, I will notify _____ at (phone) to ensure my dependent's timely removal from the study. Withdrawal of my dependent will involve no prejudice to his or her future health care or any loss of rights or benefits to which he or she is otherwise entitled. Any new significant finding developed during the course of this study which might affect my willingness to allow continued participation by my dependent will be communicated to me.

14B. The investigator may terminate my dependent's participation in this study for the following reasons: _____.

15. I understand that I am making a decision whether or not to allow the participation of my dependent in the research project described in the preceding sections subject to the conditions of participation described above. My signature indicates that I have decided to allow my dependent's participation, having read and understood the information presented above and having been given the opportunity to ask any questions that I might have about the research study or my dependent's participation in the study. Further, my signature indicates that I have been provided with a copy of this consent document and a copy of a document entitled, "California Experimental Subject's Bill of Rights."

SIGNATURES AND **DATE** SIGNED: **PRINTED** OR **TYPED IDENTIFICATION:**

_____ _____
Patient/Subject (Date) Name/Status/Sponsor's SSN

_____ _____
Parent/Legal Guardian (Date) Name/Status/SSN

_____
Relationship to Patient/Subject

_____ _____
Witness (Date) Name/Grade or Rank

_____ _____
Researcher/Investigator (Date) Name/Grade or Rank

Subject's Initials: _____

IRB Approval Stamp/Seal Required

PRIVACY ACT STATEMENT

1. Authority. 5 USC 301

2. Purpose. Medical research information will be collected to enhance basic medical knowledge or to develop tests, procedures, and equipment to improve the diagnosis, treatment, or prevention of illness, injury, or functional impairment.

3. Use. Medical research information will be used for statistical analysis and reports by the Department of the Navy, the Department of Defense, and other U.S. government agencies, provided this use is compatible with the purpose for which the information was collected. Use of the information may be granted to non-government agencies or individuals by the Chief, Bureau of Medicine and Surgery in accordance with the provisions of the Freedom of Information Act.

4. Disclosure. I understand that all information contained in this Consent Statement or derived from the medical research study described herein will be retained permanently at Naval Medical Center San Diego and salient portions thereof may be entered into my health record. I voluntarily agree to its disclosure to agencies or individuals identified in the preceding paragraph. I have been informed that failure to agree to such disclosure may negate the purposes for which the research study was conducted.

SIGNATURES AND **DATE** SIGNED: **PRINTED** OR **TYPED IDENTIFICATION:**

Patient / Subject (Date) (if Applicable)	Name / Status / Sponsor's SSN
Parent / Guardian (Date) (if Applicable)	Name / Status / SSN
Witness (Date)	Name / Grade or Rank

EXPERIMENTAL SUBJECTS BILL OF RIGHTS (CA)

Any person who is requested to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment and any drug or device to be used.

3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of appropriate alternative procedures, drugs, or devices that might be advantageous to the subject and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if any complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.

8. Be instructed that the consent to participate in the medical experiment may be withdrawn at any time, and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of a signed and dated written consent form when one is required.

10. Be given the opportunity to decide to consent or not consent to medical experiment without intervention of any element of fraud, coercion, or undue influence on the subject's decision.

11. Be assured that the subject's confidentiality will be preserved and his/her name will not be released without his/her permission.

Any questions regarding this research study should be directed to the principal investigator or associate investigators. Information is available from the Chairman, Committee for the Protection of Human Subjects, established for the protection of volunteers in research projects at this facility by calling (619)532-8125 or writing the Chairman, Committee for the Protection of Human Subjects at Naval Medical Center, Clinical Investigation Department (KCA), San Diego, CA 92134-5000.

TITLE 32--NATIONAL DEFENSE PART 219--PROTECTION OF HUMAN SUBJECTS—

WAIVER OR MODIFICATION OF INFORMED CONSENT DOCUMENT

32 CFR 219.116(d)
"An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation."

32 CFR 219.117(c)
"An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research."

TITLE 32--NATIONAL DEFENSE PART 219--PROTECTION OF HUMAN SUBJECTS-

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(3) The research could not practicably be carried out without the waiver or alteration; and

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(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research."

Periodic Review for CIP #«CIP» Due: «Next_Rvw_Date»

RESEARCH PROTOCOL PERIODIC CONTINUING REVIEW/REPORT FOR THE INSTITUTIONAL REVIEW BOARD (IRB)

Protocol CIP# «CIP»

Title: "«TITLE_of_Project»"

Principal Investigator (PI): «NameTitle»

Location where study is being performed: _____

Original approval date: «Appvl_Date»

Progress review for period from: «Last_Rvw_Date» to «Next_Rvw_Date»

IRB Reviewer: _____
Name, Rank, Corps

The information provided below will be used as the basis for determining whether protocol approval will continue.

CIRCLE RESPONSES BELOW

1. Have there been changes (modifications or amendments) to the study during this reporting period? YES* NO

a. If YES, have the changes been reported to the IRB? YES NO N/A

b. If YES, summarize the changes, and comment specifically on whether the changes alter the risk to study subjects: (use additional pages if required)

_____

_____

_____

_____

_____

2. Have any adverse or unexpected events occurred during this reporting period? YES* NO

a. If YES, have all been reported to the IRB? YES NO N/A

b. If YES, summarize the events, and comment specifically on whether the events alter the risk to study subjects: (use additional pages if required)

_____

_____

_____

_____

_____

3. Have any of the investigators been changed (added or removed)? YES* NO

a. If investigators have been added, have an updated "Key Personnel" list and signed "Human Use Assurance Statement" been submitted to the IRB? YES NO N/A

b. If investigators have been removed, has a memo to this effect been submitted? YES NO N/A

c. If the PI has changed, has the existing subject data been transferred to the new PI? YES NO N/A

4. If this study has been designated as more than minimal risk, does the protocol include a list of the medical monitor's responsibilities that has been signed by the medical monitor? YES NO* N/A

If NO, attach this document.

Periodic Review for CIP #«CIP» Due: «Next_Rvw_Date»

5. Was patient accessioning suspended during this reporting period for any reason? YES* NO N/A

If YES, explain why on an attached page.

6. Did any subjects withdraw during this reporting period? YES* NO N/A

If YES, explain why on an attached page.

7. Attach a copy of the currently approved informed consent document (ICD). Have there been any changes to the study, adverse events reported, or any other matters that warrant changes to this ICD? YES* NO N/A

If YES, explain on an attached page.

8. Are copies of the signed informed consent document being appropriately filed? YES* NO N/A
(The patient must receive a copy, the investigator must maintain a copy, and the original must be placed in the patient's health record)

If NO, explain on an attached page.

9. Are adequate security measures in place to prevent unauthorized access to the patient identifiers? YES NO* N/A

If NO, explain on an attached page.

10. Do the potential benefits of the study continue to outweigh the risks? YES NO*

If NO, explain on an attached page.

11. Are all safeguards required by the IRB still adequate and in place? YES NO*

If NO, explain on an attached page.

12. Summarize the findings of this study during this reporting period: (use additional pages if required)

13. Describe any unforeseen delay in the conduct of this study: (use additional pages if required)

14. List all publications, abstracts and presentations from this study during this reporting period: (use additional pages if required)

15. What is the status of patient enrollment? OPEN CLOSED

16. Is the budget request current? YES NO* N/A

If NO, attach an amended budget request.

17. Do you wish to terminate or to complete this project at this time? YES* NO

Periodic Review for CIP #«CIP» Due: «Next_Rvw_Date»

18. If YES, explain why on attached page

SUMMARY

«AUTH Pts» Number of patients authorized for enrollment in this study
_____ Number of patients enrolled previously
_____ Number of patients enrolled this reporting period. Attach a list of subjects accrued during this reporting period using only their initials and SSN.
_____ TOTAL number of patients enrolled in the study
_____ Current number of patients in follow-up

I certify that the information provided herein is correct and accurate to the best of my knowledge.

INVESTIGATOR'S SIGNATURE/DATE: _____

IRB Reviewer Summary:

Based on review of the information submitted by the PI, the audit and review, the following discrepancies were noted:

_____
_____
_____
_____
_____

The level of risk currently assigned to this study is «RISK_Category».

The level of risk should be CHANGED. {if YES, circle one below} YES NO

1) No more than Minimal (Minimal); or
2) More than Minimal (>Minimal).

Based on my review, I recommend the subject protocol be approved by the IRB for: Circle one. If recommending suspension or termination, explain.

CONTINUATION COMPLETION SUSPENSION TERMINATION

_____
_____
_____
_____
_____
_____

Signature IRB Reviewer Date

DATABASE Comments: «COMMENTS»

_____
_____
_____

CLINICAL INVESTIGATION COMPLETION REPORT

1. **CIP #**_____ Date:_____

2. Principal Investigator: _____

3. Project Title:

4. Location of Study: (e.g., NMCSD, Internal Medicine Department)

_____

5. Date Protocol **Approved**: _____

6. Date Protocol **Initiated**: _____

7. Date Protocol **Completed**: _____

8. State **objectives** of study:

_____

_____

_____

_____

_____

9. State **findings** of study:

_____

_____

_____

_____

_____

10. For **HUMAN** use studies, report the following:

a. Number of subjects enrolled **since last continuing review**:_____
b. **Total** number of subjects enrolled in study: _____

Attach a list of initials and SSNs of **all** subjects enrolled in this study.

11. Has all follow-up of subjects been completed? ____
(If not, study is not complete)

12. For **ANIMAL** Use Studies, Report the Following: Precise number of each species used in the study.

a. Species: _____
b. Total number of animals used: _____

13. As a result of this project:

a. List **manuscripts** published or submitted for publication from this study. Format: Authors. Title. Journal year; volume: pages.

_____

_____

_____

b. List **abstracts** published or submitted for publication from this study. Format: Authors. Title. Journal year; volume: pages.

c. List **presentations** from this study. Format: Society, City, Date.

Signature of Principal Investigator

From BUMEDINST 6000.12A:

What Is and Is Not A Clinical Investigation

Clinical investigation is any research program, project, task, test, experiment, record review, evaluation, or similar undertaking that uses data collected from DoD health care beneficiaries, laboratory animals, or *in vitro* to study the maintenance of health or the prevention, alleviation or cure of disease, and whose primary purpose is designed with the intent to develop or contribute to generalizable knowledge.

1. Certain biomedical or health care system projects may use scientific methods or involve the collection and/or statistical analysis of health data, but do not qualify as Navy CIP projects. They include, but are not limited to:

a. Activities that are designed to assess or improve the health care delivery system, such as:

(1) Surveys/questionnaires to staff or patients regarding opinions/preferences about the use of treatments, facilities, processes, practices, satisfaction or quality of care.

(2) Assessments of need for, or effectiveness of, staff educational programs.

(3) Cost effectiveness or process efficiency projects.

b. Case reports of clinical experiences and/or descriptions of new procedures/approaches.

c. Literature reviews.

d. Establishment of registries (populating databases) for unspecified uses in future studies that will require the preparation and submission of study-specific protocols.

e. Epidemiological surveillance or other epidemiological practices (versus epidemiological research) designed primarily to protect or enhance the health of broadly defined populations.

2. A project may not qualify for inclusion in the CIP but still may meet the definition of "research involving human subjects" and need to be reviewed consistent with 32 CFR 219 and prevailing Navy policies for protection of human subjects.

3. Regardless of whether the provisions of 32 CFR 219 pertain to projects excluded from the CIP, the technical approach of all projects should give appropriate consideration to the privacy of all individuals concerned and to the confidentiality of their data.

Categories of Research That May Be Expedited

Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure[1] (63 FR 60364-60367, November 9, 1998)

Applicability

1. Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 32 CFR 219.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

2. The categories in this list apply regardless of the age of subjects, except as noted.

3. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

4. The expedited review procedure may not be used for classified research involving human subjects.

5. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.

6. Categories one through seven pertain to both initial and continuing IRB review.

Research Categories

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a. From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an eight week period and collection may not occur more frequently than two times per week; or

b. From other adults and children[2], considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an eight week period and collection may not occur more frequently than two times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means.

Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the

membrane prior to or during labor; (h) supra - and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the DOD regulations for the protection of human subjects. 32 CFR 219.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research

employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the DOD regulations for the protection of human subjects. 32 CFR 219.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the convened IRB as follows:

a. Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

b. Where no subjects have been enrolled and no additional risks have been identified; or

c. Where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

---

[1] An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 32 CFR 219.110.

[2] Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402(a).

Categories of Research That May Be Exempt

TITLE 32--NATIONAL DEFENSE PART 219--PROTECTION OF HUMAN SUBJECTS—

Sec. 219.101 To what does this policy apply?

(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are **exempt** from this policy:

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if: (i) The human subjects are elected or appointed public officials or candidates for public office; or (ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(4) Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic

specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine: (i) Public benefit or service programs; (ii) Procedures for obtaining benefits or services under those programs; (iii) Possible changes in or alternatives to those programs or procedures; or (iv) Possible changes in methods or levels of payment for benefits or services under those programs.

(6) Taste and food quality evaluation and consumer acceptance studies, (i) If wholesome foods without additives are consumed or (ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

INSTRUCTIONS
HUMAN RESEARCH PROTOCOL PROPOSAL

General instructions: These notes are designed to assist users with the accompanying on-disk Human Research Protocol Proposal. Please fill in the data requested. If an area does not apply to your proposal, type "N/A." NOTE: Human research protocols are those which involve the collection/analysis of data obtained either directly from individuals or indirectly from records or specimens.

TABLE OF CONTENTS (FOR INSTRUCTIONS)

HUMAN RESEARCH PROTOCOL PROPOSAL COVER SHEET

Type in all requested information (except shaded areas) including:

Title	Enter the full title of the proposal.
CIP #	Obtain CIP # from CID staff and type in.
Principal Investigator*	Enter all info for PI.
Number of Human Subjects	Enter the maximum to be enrolled in each category.
IRB Review Section	Will be filled in by CID staff.
Retrovirology Research	Type "YES" or "NONE".
Investigational Drugs, Devices, or Biologics	Enter the Drug/Device/Biologic - or type "NONE".
IND # or IDE #	Will be filled in by CID staff.
Personnel/Environmental Hazards	Enter hazard type including use of radiation or lasers – or "NONE".
Proposed Start Date/Duration	Enter the start date and duration of study.
Budget	Fill in specific fiscal years and dollar amounts.
CRADA/MOU	Will be filled in by CID staff.
Signatures	Obtain original signatures for PI, Department Chair
Principal Investigator*	Type in the name in box to left of "date.".
Department	Enter in the PI's Department Name.
Department Chairman	Type the PI's Chair's name in box to left of "date."
Commanding Officer (if satellite site)	If non-NMCSD facility, obtain signature from CO of satellite facility

- **If PI is from another facility, use PI (A) ("PI for Administrative Purposes")**

Table Of Contents

Do not alter Table of Contents. Page numbers will update automatically as you fill in remaining sections.

Header Information

A shortened title, the PI's name, and the protocol (CIP) number must be entered into the existing header as a single line of text. Double click on the header line at this time and make the changes.

I. PROJECT SUMMARY

A. **ABSTRACT**: Type a structured abstract in the box provided.
   1. The abstract should be one succinct paragraph (not exceeding one page), able to stand alone as a description of the proposed work when separated from the remainder of the proposal. Use language that non-specialists can understand. Spell out abbreviations and do not cite references in the abstract.
   2. Include:
      - Brief summary of the Background of the problem or issue addressed by the protocol.
      - Objective(s) of the study.
      - The research design and study methods.
      - Potential impact or applicability of the anticipated results.
      - Summary of planned analysis

B. **KEY WORDS**: Type key words in the boxes provided.
   1. List a maximum of 10 words used to search for similar and related research work through MEDLINE.

C. **ABBREVIATIONS USED**: Type all abbreviations and their meanings.

D. **KEY PERSONNEL**:
   1. Enter data specified in the column headings for each member of the study team.

2. Delete extra rows in the table as follows: With the cursor located anywhere on the row to be deleted select "Table" then "Select Row" and finally, click on the delete icon (scissors).
3. Add more rows in the table as follows: Place the cursor on the bottom row, select "Table," then "Insert Rows."

E. **SUB-INVESTIGATORS**:
1. Enter data requested.

II. PROJECT DESCRIPTION. Use language that non-specialists can understand. Cite references by superscript number in order of appearance in the text.

A. **BACKGROUND AND SIGNIFICANCE**: Provide a detailed description (one to two pages) of the background to the proposal.
1. What led you to propose this study?
   - Describe existing knowledge noting discrepancies, inaccuracies, and controversies.
   - Identify the gaps in knowledge your project is intended to fill.

B. **SPECIFIC OBJECTIVES**: State the specific question(s) the study will attempt to answer.

C. **PREVIOUS WORK BY YOU RELATED TO PROPOSAL**:
1. If none, state "None."
2. Provide an account of the relevant studies or preliminary work **conducted by the PI or AIs** establishing the experience and competence of the team in the proposed area of work.
3. Include in the Appendix (as needed) reprints, preprints, figures, diagrams, etc. to demonstrate the investigators' experience and competence to perform the proposed work.

D. **RESEARCH DESIGN**:
1. **General Approach**: List all methodological words that indicate the broad techniques and approaches that will be used in the proposed work. Examples: retrospective, prospective, chart review, randomized, blinded, cross-over, clinical trial, case-control.
2. **Subject Population**: Identify the subject population with inclusion and exclusion criteria.
3. **Methods**: Discuss in as much detail as possible the experimental design, methods and procedures planned to accomplish each specific objective of the project. This discussion must be sufficiently detailed, including appropriate citations, to allow valid scientific review.
4. **Retrovirology Research**: NOTE: If not applicable, type "N/A," or if applicable:
   - Provide any additional information not already presented in the methods section.
   - Ensure that all protocols have been reviewed and approved by BUMED HIV Program Division (MED-O2H) prior to IRB review. (Attach a copy of review.)
5. **Investigational Drugs/Devices/Biologics Research**: NOTE: If not applicable, type "N/A," or if applicable:
   - Describe in detail the proposed use of any investigational drug, device, or biological agent. Note that this includes not only agents which are not FDA approved, but also agents which are FDA approved but are being studied for an "off label" indication, route, dose or combination, even when such use would be legal in an individual patient. Such use requires an IND (investigational new drug) or IDE (investigational device exemption) from the FDA.
6. **Statistical Analysis**: Explain how the sample size was derived, including statistical power calculations. Explain the specific statistical technique(s) to be used to analyze data collected.
7. **Military Relevance/Operational Use**:

- Describe any specific military or operational use for the proposed work. If none, state "None."

8. **Data Collection Sheet and Questionnaire** (required for all studies)
   - All data collection sheets, questionnaires, or other exhibits must be included. A subject logbook with identifying information (name, FMP/SSN, demographics) must be kept separate from the data collection sheet. All subjects must be assigned an identifying number which will be coded to the information in the logbook (-no linkable patient identifiers are allowed on data collection sheets). This is designed to protect the privacy of research subjects. The log is required to be presented at the continuing review along with the signed patient consent forms.

III. BIBLIOGRAPHY

A. List all references cited in the proposal in order of appearance in text under this section using the Uniform Requirements Style. In the body of the text use superscript reference numbers only. EXAMPLES (If six or fewer authors, list all; if seven or more, list first six and add et al.:
   Ref #. Author(s). Title. Journal, year; volume number (number):pages.
   Format for periodical references:
   Pullon PA, McGivney J. Computer utilization in an oral biopsy service. Int J Oral Surg 1977;6:251-5.
   Format for book references:
   Seakins J, Saunders R, editors. Treatment of inborn errors of metabolism. London:Churchill Livingstone; 1973. P. 51-6.
   Format for chapter references:
   Hudson FB, Hawcroft J. Duration of treatment in phenylketonuria. In: Seakins J, Saunders R, editors. Treatment of inborn errors of metabolism. London: Churchill Livingstone; 1973. p. 51-6.

IV. CURRICULUM VITAE

A. ATTACH A CURRENT (DATED) CV FOR EACH PI AND AI.

V. SPECIAL INFORMATION AND SUPPLEMENTARY DOCUMENTATION

[If these items are not applicable to your project, type "N/A."]

A. COLLABORATION WITH OTHER INDIVIDUALS OR INSTITUTIONS
   1. Provide a detailed explanation of any proposed arrangements. Attach any written communications confirming the proposed arrangements.
   2. Describe the research efforts proposed to be performed by outside contractors.
   3. List names of individuals (include addresses & phone numbers) proposed to participate in scientific consultations for outside expert advice and support of research endeavor.

   SPECIAL NOTE: Do not make any commitments for participation, equipment, funds, etc. to any outside organization. Such arrangements will be made by CID through Cooperative Research and Development Agreements (CRADAs) or Memoranda of Understanding (MOUs).

B. PERSONNEL AND ENVIRONMENTAL HAZARDS/PRECAUTIONS:
   1. State either:

- "No proposed material, chemicals, infectious organisms, or situations limited to this research will produce personnel or environmental hazards."
  OR
- "Safety programs and procedures have been established and implemented to eliminate and minimize hazards to personnel and the environment." (NOTE: This statement may be used only if you are proposing to use procedures and protocols that can be considered routine procedures and adequate safety precautions are already in place).
  OR
- Enumerate the potential hazards to subjects, investigators or the environment associated with this proposal (e.g., viral agents, toxins, radioisotopes, oncogenic viruses, chemical carcinogens, etc.). Explain any safety precautions, surveillance procedures in place to monitor potential exposures (e.g., laser protective eyewear, dosimetry badges, etc.), and/or engineering controls used these subjects.

2. The command Safety Committee must review and approve the proposal if there are any situations that produce hazards beyond routine exposures. The Radiation Safety Committee or Laser Use Committee must review and approve the proposals involving the use of radiation or lasers.

C. **APPLICATION TO USE HUMAN SUBJECTS (OR EXEMPTION):** This entire section must be stated in lay-language understandable by non-medical personnel. Research involving the use of human subjects is any study that uses research material obtained for individually-identifiable living human subjects in the form of specimens, records, or data. All such human research must be adequately justified. Some studies may be exempted by the Institutional Review Board. If your study involves only questionnaires, interviews, or strictly retrospective review of existing data where patient identifiers are not recorded, it may qualify for such an exemption. If you think your study may qualify as exempt, check with CID before completing this section.

1. **Subject Objectives:** What specific question(s) will the study attempt to answer?
2. **Subject Population:** Describe the characteristics of the subject population, such as the anticipated number, age ranges, sex, ethnic background, military or civilian, military health beneficiary status, and health status. The rationale for the use or exclusion of special classes of subjects, such as pregnant women, children, or others who are likely to be vulnerable must be explained. Briefly state why the study should be performed in humans rather than an animal or *in vitro* model.

   Under separate headings, specifically list:

   SUBJECT INCLUSION CRITERIA
   SUBJECT EXCLUSION CRITERIA

3. **Experimental Procedure(s):** Briefly describe the experimental procedure(s) proposed to accomplish the specific objective(s).
4. **Research Material Collected:** Identify the sources of research material to be obtained from individually-identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes, or whether use will be made of existing specimens, records, or data. If data collection will be in conjunction with other accepted procedures, specify what, if any, portions of the data to be collected will be derived from experimental procedures.
5. **Privacy:** Describe details for protecting subjects' privacy. Specify how anonymity will be maintained for any human data to be collected, including coding of data sheets. Subject names and identifiers may not be associated with the data collected from the subject (coded data sheets should be used). Consider applicable language below relative to experimental data, consent forms, and related documents:

   "All documents relating to an individual's participation in this study will be kept in a locked storage file to which only the

Principal Investigator and designated assistants will have access. Computer data files will be stored in a password-protected computer system. No individual medical records will be retained for this study. At the end of the study, all data sheets will be destroyed/shredded and all other data will be stored in the Principal Investigator's password-protected computer until data analysis is complete."

6. **Subject Recruiting:** Describe plans for recruiting subjects and the consent procedures to be followed, including the circumstances under which consent will be sought, how subjects will be contacted, who (by name) will seek it, the information to be provided to prospective subjects, and the method of documenting consent. Describe procedures for obtaining assent from minors if applicable. Describe specific procedures for avoiding coercion of subjects to participate, especially of vulnerable populations. Vulnerable populations specifically include active duty members, especially those in high stress training environments such as boot camp. In addition to other specific measures, consider using the following: "For research involving military personnel, unit officers and noncommissioned officers (NCOs) shall not influence the decisions of their subordinates to participate or not participate as research subjects. Unit officers and senior NCOs in the chain of command shall not be present at the time of solicitation and consent during research recruitment session in which members of units under their command are afforded the opportunity to participate as research subjects. When applicable, officers and NCOs so excluded shall be afforded the opportunity to participate as research subjects in a separate recruitment sessions. At all such unit recruitment sessions, an ombudsman not connected in any way with the proposed research shall be present to monitor that the voluntary nature of participation is adequately stressed and that the information provided about the research is adequate and accurate."
7. **Risks:** Describe any potential risks (listed from the most to the least significant): physical, psychological, social or other, and assess their likelihood and seriousness. Describe alternative treatments and/or procedures that might be appropriate for use on the subjects. Delineate risks which may be a normal part of treating an individual from those which are performed solely for the purposes of the proposed study.
8. **Radiation or Laser Exposure:** Will the subjects be exposed to radiation or laser use that is not part of their standard treatment? If yes, specify.
9. **Justification of risks:** Any anticipated benefits to the subject population must be specifically identified. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result.
10. **Minimization of Risks:** Describe the procedures for protecting against or minimizing any potential risks, and assess their likely effectiveness. Discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Also, describe the provisions for monitoring the data collected to ensure the safety of subjects.
11. **Medical Monitor:** The name of the medical monitor responsible for safety must be provided. The medical monitor may not be a member of the investigational team. If the study is deemed greater than minimal risk, the monitor must be a physician or dentist. Consider applicable sample language below (use only one version):

    - **Multicenter Trial Version**

"This multicenter clinical trial will be monitored by the sponsor for protocol compliance and adverse risk to the subjects. Dr. Joe Smith, LCDR, MC, USN will be the NMCSD medical monitor for this protocol. In this capacity, Dr. Smith will be cognizant of the medical welfare of the NMCSD enrolled subjects. He/she will be informed of the enrollment, progress, and treatment of these subjects and apprised of any unanticipated adverse events to ensure protection of the subjects from excessive risk. He/she has the authority to recommend suspension or disenrollment or any other steps deemed necessary to protect the subjects. Dr. Smith's clinical skills and experience make him/her well suited to this task."

- **NMCSD-Only Study Version**
  "Dr. Joe Smith, LCDR, MC, USN will be the NMCSD medical monitor for this protocol. In this capacity, Dr. Smith will be cognizant of the medical welfare of the enrolled subjects. In this capacity he/she will perform the following functions to ensure protection from excessive risk:
  a. Monitor the consent process to ensure an absence of coercion
  b. Monitor data collection and clinical outcome
  c. Be apprised of unexpected adverse event reports
  d. Make sure inclusion/exclusion criteria are followed
  e. Review data security measures
  f. Have full access to study data

  Dr. Smith has the authority to recommend suspension or disenrollment or any other steps deemed necessary to protect the subjects. Dr. Smith's clinical skills and experience make him/her well suited to this task."

D. HUMAN USE ASSURANCE STATEMENT: Obtain copies of the cited documents from CID to read. Enter data and obtain signatures.

E. INSERT CONSENT FORM (template on separate disk provided by CID - includes the Privacy Act Statement and California Experimental Subjects Bill of Rights), **INFORMATION SHEET, OR WAIVER.**

VI. BUDGET

A. **BUDGET SUMMARY:** Enter the applicable Fiscal Years (FYs) and dollar amounts.

B. **DETAILED BUDGET LIST:** List specific items and dollar amounts in each category.

VII. APPENDIX

A. **REVIEW SIGNATURES:** Will be completed by CID staff.

B. **DEPARTMENT SUPPORT STATEMENT:** Describe all support required from, and impact on, any other department. State "N/A" for those departments with no involvement.

C. **COMMITTEE MINUTES:** Will be inserted by CID.

Shortened Title of Proposal

HUMAN RESEARCH PROTOCOL PROPOSAL

Cover Sheet

Use accompanying instructions. [CID staff will fill in shaded areas.]

Title:				
CIP #:				
Principal Investigator (PI or PI(A))	**Last Name:**	**First Name:**	**MI:**	**Rank or Degree:**
	Department/Division:	**Department Code:**		
Naval Medical Center San Diego, San Diego, CA 92134-5000				
DOD Assurance Number: DOD40005	**E-Mail Address:**			
Phone:	**DSN:**	**Fax:**	**Fax DSN:**	
NUMBER OF HUMAN SUBJECTS **TOTAL:**	**Control:**	**Experimental:**	**Minors:**	
Reviewed and approved by the IRB in accordance with the common rule and other governing regulations.				
Date of IRB Review:	**Risk Category:**			
Chairman, IRB Approval:	( ) **K. Earhart, CDR, MC, USN** **(Date)**			
Retrovirology Research:				
Investigational Drugs, Devices, or Biologics:	**IND/IDE #**			
Personnel/Environmental Hazards:				
Proposed Start Date/Duration:				
Budget **FY:** $	**FY:** $	**FY:** $	**Total:** $	
CRADA/MOU (Yes or No):	**If Yes, Name:**			

Signatures: We accept responsibility for the conduct of the project, as specified in the attached assurance statement, and agree to provide any required progress reports.

	Date			Date
Principal Investigator		**Department**	**Department Chair**	

The officials signing below certify that the information provided within this document is correct, and that, as required, future reviews will be performed, and certification will be provided.

	Date	**John M. Kelso, CDR, MC, USN**	Date
Commanding Officer (if satellite site)		**By Direction of the Commander**	

TABLE OF CONTENTS

Shortened Title of Proposal *Name of PI* *CIP #*

I. PROJECT SUMMARY

A. ABSTRACT:

B. KEY WORDS:

C. ABBREVIATIONS USED:

Shortened Title of Proposal *Name of PI* *CIP #*

D. KEY PERSONNEL

	• Name, Degree & Grade/Rank • Social Security # • Phone # • Pager #	• PI, AI, or PI(A)* • PRD • % of Time Devoted to this Effort	• Organization (e.g. NMCSD) • Department • Status (Staff, Trainee, etc.)
(1)			
(2)			
(3)			
(4)			
(5)			
(6)			
(7)			
(8)			

* ***PI*** = Principal Investigator
PI (A) = The local Principal Investigator for Administrative purposes (use only if PI is from another facility
AI = Associate Investigator

NOTE: THE FOLLOWING IS TO BE COMPLETED BY CID STAFF.
This is the ☐ Original or ☐ Updated (check one) key personnel listing.

Date Effective: _____

E. SUB-INVESTIGATORS

Sub-investigators are individuals who will be trained in the specifics of the protocol and on how to perform the informed consent process from prospective subjects. This does not require the submission of a curriculum vitae or listing them as investigators on the Human Use Assurance Statement. However, the Principal Investigator will be responsible for providing training to all Sub-Investigators and documenting such by listing the names below. **Prior approval must be obtained from the IRB, before Sub-Investigators can be utilized. Approval can be requested by completing this form and including it with the protocol submission.** If approved, the information must be updated at the time of continuing review.

1. Will anyone other than the Key Personnel be performing the consent process? (Check one.)
   ☐ **Yes** ☐ **No**

If Yes, provide justification:

Category (Residents, Staff, Civilian):

2. Provide Names and SSNs for all Sub-Investigators in the table below.

The following individuals will be sub-investigators on this study. All have/will participate(d) in, and satisfactorily complete(d), training in the specifics of this protocol, as well as how to appropriately obtain informed consent form prospective subjects.

PRINTED NAME	SSN

PRINTED NAME	SSN

Shortened Title of Proposal *Name of PI* *CIP #*

II. PROJECT DESCRIPTION

A. BACKGROUND AND SIGNIFICANCE:

B. SPECIFIC OBJECTIVES:

C. PREVIOUS WORK BY YOU RELATED TO PROPOSAL:

D. RESEARCH DESIGN

1. General Approach:

2. Subject Population (with inclusion/exclusion criteria):

3. Methods:

4. Retrovirology Research:

5. Investigational Drugs/Devices/Biologics Research:

6. Statistical Analysis:

7. MILITARY RELEVANCE/OPERATIONAL USE, IF ANY:

8. DATA COLLECTION SHEET(S) AND QUESTIONNAIRES:

Insert hard copy of all data collection sheets and questionnaires.

III. BIBLIOGRAPHY

IV. CURRICULUM VITAE

Insert hard copy of current CV for each PI and AI.

V. SPECIAL INFORMATION AND SUPPLEMENTARY DOCUMENTATION

A. COLLABORATION WITH OTHER INDIVIDUALS OR INSTITUTIONS: COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENTS (CRADAs) AND MEMORANDA OF UNDERSTANDING (MOUs).

B. PERSONNEL AND ENVIRONMENTAL HAZARDS/PRECAUTIONS:

Shortened Title of Proposal *Name of PI* *CIP #*

C. APPLICATION TO USE HUMAN SUBJECTS

1. **Specific Objectives:**

2. **Subject Population:**

   a. **Subject Inclusion Criteria:**

   b. **Subject Exclusion Criteria:**

3. **Experimental Procedure(s):**

4. **Research Material Collected:**

5. **Privacy**

6. **Subject Recruiting:**

7. **Risks:**

8. **Radiation or Laser Exposure:**

9. **Justification of Risks:**

10. **Minimization of Risks:**

11. **Medical Monitor:**

Shortened Title of Proposal *Name of PI* *CIP #*

D. HUMAN USE ASSURANCE STATEMENT

We, the Principal Investigator, and Associate Investigators on the above noted research project have read and understand the provisions of 32 CFR Part 219 (Protection of Human Subjects), the Belmont Report (Ethical Principles and Guidelines for the Protection of Human Subjects of Research), NAVMEDCEN SDIEGOINST 6500.9 (Human Clinical Investigation Program, Institutional Review Board, and the Protection of Human Subjects) and, if applicable, 45 CFR 46 Subpart B (Additional Protections Pertaining to Research Involving Fetuses, Pregnant Women, and In Vitro Fertilization) and Subpart D (Additional Protections for Children Involved as Subjects in Research). The DOD Multiple Project Assurance Number for this facility is DOD40005. We agree to abide by all applicable laws and regulations and agree that in all cases the most restrictive regulation related to a given aspect of research involving protection of research volunteers will be followed during the conduct of this research project. In the event that we have a question regarding our obligations during the conduct of this Navy sponsored project, we have ready access to each of these regulations, as either a personal copy or available on file from the Chairman, Committee for the Protection of Human Subjects. We understand that the immediate resource for clarification of any issues related to the protection of research volunteers is the Chairman of that committee. We understand that failure to comply with reporting and/or review requirements will require suspension or termination of the project.

PRINT NAME, RANK/DEGREE	POSITION OR ROLE (PI, AI)	SIGNATURE	DATE

E. CONSENT FORM, INFORMATION SHEET, OR WAIVER

Insert hard copy of appropriate documents.

Shortened Title of Proposal *Name of PI* *CIP #*

VI. BUDGET

A. BUDGET SUMMARY:

BUDGET ITEM	Yr 1 $ FY:	Yr 2 $ FY:	Yr 3 $ FY:
Personnel Costs			
Minor Equipment Costs < $25K)			
Major Equipment Costs (≥ $25K)			
Equipment Maintenance Costs			
Equipment LEASE Costs			
Expendable Supplies			
Animal Purchase and Per Diem			
Miscellaneous Expenses (including printing, reproduction, and publication)			
Travel (for data collection)			
Contracts/Consultants			
TOTAL:			

A detailed list of items requested FOR EACH YEAR is included on the following page.

FUNDING SOURCE(S)

In-House (CID)			
Other DOD: (Specify)			
HMJFAMM			
Grant: (Specify)			
Gift: (Specify)			
CRADA (Specify company)			

B. DETAILED BUDGET LIST

YEAR 1 BUDGET

BUDGET ITEM	DOLLAR AMOUNT
Personnel Costs:	
Minor Equipment Costs < $25K):	
Major Equipment Costs (≥ $25K):	
Equipment Maintenance Costs:	
Equipment LEASE Costs:	
Expendable Supplies:	
Miscellaneous Expenses (including printing, reproduction, and publication):	
Travel (for data collection):	
Contracts/Consultants:	
YEAR 1 TOTAL:	

Shortened Title of Proposal *Name of PI* *CIP #*

YEAR 2 BUDGET

BUDGET ITEM	DOLLAR AMOUNT
Personnel Costs:	
Minor Equipment Costs < $25K):	
Major Equipment Costs (≥ $25K):	
Equipment Maintenance Costs:	
Equipment LEASE Costs:	
Expendable Supplies:	
Miscellaneous Expenses (including printing, reproduction, and publication):	
Travel (for data collection):	
Contracts/Consultants:	
YEAR 2 TOTAL:	

Shortened Title of Proposal *Name of PI* *CIP #*

YEAR 3 BUDGET

BUDGET ITEM	DOLLAR AMOUNT
Personnel Costs:	
Minor Equipment Costs < $25K):	
Major Equipment Costs (≥ $25K):	
Equipment Maintenance Costs:	
Equipment LEASE Costs:	
Expendable Supplies:	
Miscellaneous Expenses (including printing, reproduction, and publication):	
Travel (for data collection):	
Contracts/Consultants:	
YEAR 3 TOTAL:	

VII. APPENDIX

A. REVIEW SIGNATURES

The proposed research involves reviews and/or approvals by the committees and organizations noted below.

	YES	NO		APPROVAL DATES:		INITIAL
				PENDING	APPROVED	
1. HUMAN SUBJECTS			IRB			
2. RETROVIRUS			MED-O2H			
3. INVESTIGATIONAL AGENT			FDA			
4. RADIATION/LASER			RSC/LUC			
5. COLLABORATION			CRADA/MOU			

(CID will complete approval dates.)

The following signatures indicate the documentation has been reviewed and has been completed appropriately according to the best knowledge of the signees.

CID Program Administrator

Lynda J. Reed, CIP (Signature)	**Date**

Director, CID w/CO Naval Medical Center San Diego by direction authority

CDR J.M. KELSO, MC, USN (Signature)	**(Date)**

Action by BUMED reviewing authority NOT applicable.

B. DEPARTMENT SUPPORT STATEMENT

The proposed project may impact other departments within the organization. Provide a statement of the support needed from the department(s) listed below in order to perform the study.

LABORATORY:

PHARMACY:

RADIOLOGY:

NUCLEAR MEDICINE:

NURSING SERVICES:

PATIENT ADMINISTRATION:

PATIENTS (i.e. # of admissions):

BED OCCUPANCY/DURATION OF STAY:

OTHER SPECIAL REQUIREMENTS:

SIGNATURES: We agree to provide the support described above.

Signature **Name:** **Rank:** **Title:**	**Signature** **Name:** **Rank:** **Title:**
Signature **Name:** **Rank:** **Title:**	**Signature** **Name:** **Rank:** **Title:**

C. INSERT: **COMMITTEE MINUTES** signed by Chairman, IRB, and Deputy Commander

ADVERSE EVENT REPORT

Date: _____

CIP #_____ PI NAME _____
Last, First, MI, Rank

Patient ID# _____

Investigational Agent _____

Date of Event _____ Location of Event _____

Adverse Event

_____
_____
_____
_____
_____
_____
_____
_____
_____

Was the adverse event related to the study drug? _____Unlikely
_____Possible
_____Probable

What was the outcome of the adverse event? _____
_____
_____
_____
_____

Has this event been reported to the pharmaceutical company?____
_____
_____

Investigator Signature: _____
Last First MI Rank

TABLE OF ACRONYMS

AI	Associate Investigator
BUMED	Bureau of Medicine and Surgery
CFR	Code of Federal Regulations
CID	Clinical Investigation Department
CIP	Clinical Investigation Program
CO	Commanding Officer
DOD	Department of Defense
DTF	Dental Treatment Facility (military)
FDA	Food and Drug Administration
HHS	Department of Health and Human Services
ICD	Informed Consent Document
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
MTF	Medical Treatment Facility (military)
NIH	National Institutes of Health
NMCSD	Naval Medical Center San Diego
NSHS	Naval School of Health Sciences
OHRP	Office for Human Research Protections
PI	Principal Investigator
SOP	Standard Operating Procedure
SECNAV	Secretary of the Navy
USC	United States Code